- 8 Louis WJ, Tabei R, Spector S. Effects of sodium intake on inherited hypertension in the rat. *Lancet* 1971;ii:1283-6.
- 9 George CF, Lewis PJ, Petrie A. Clinical experience with the use of an ultrasound sphygmomanometer. *Br Heart J* 1975;37:804-7.
- 10 Roulston JE, MacGregor GA. Measurement of plasma renin activity by radioimmunoassay after prolonged cold storage. *Clin Chim Acta* 1978;88:45-8.
- 11 James VHT, Wilson GA. Determination of aldosterone in biological fluids. In: Reid E, ed. *Assay of drugs and other trace compounds in biological fluids. Methodological development in biochemistry*. Vol 5. Amsterdam: Elsevier, 1976:149-58.
- 12 Khaw KT, Rose G. Population study of blood pressure and associated factors in St Lucia, West Indies. *Int J Epidemiol* 1982;11:372-7.
- 13 Simmons D. Blood pressure, ethnic group, and salt intake in Belize. *J Epidemiol Community Health* 1983;37:38-42.
- 14 Smith SJ, Markandu ND, Sagnella GA, Poston L, Hilton PJ, MacGregor GA. Does potassium lower blood pressure by increasing sodium excretion? A metabolic study in patients with mild to moderate essential hypertension. *Journal of Hypertension* 1983;1, suppl 2:27-30.
- 15 Brunner HR, Baer LB, Sealey JE, Ledingham JGG, Laragh JH. The influence of potassium administration and of potassium deprivation on plasma renin in normal and hypertensive subjects. *J Clin Invest* 1970;49:2128-38.
- 16 Beard TC, Cooke HM, Gray WR, Barge R. Randomised controlled trial of a no-added-sodium diet for mild hypertension. *Lancet* 1982;ii:455-8.
- 17 Erwtentant M, Nagelkerke N, Lubsen J, Koster M, Dunning AJ. β Blockade, diuretics, and salt restriction for the management of mild hypertension: a randomised double blind trial. *Br Med J* 1984;289:406-9.
- 18 Watt GCM, Edwards C, Hart JT, Hart M, Walton P, Roy CJW. Dietary sodium restriction of mild hypertension in general practice. *Br Med J* 1983;286:432-6.
- 19 Richards AM, Nicholls MG, Espirer EA, et al. Blood pressure response to moderate sodium restriction and to potassium supplementation in mild essential hypertension. *Lancet* 1984;ii:757-61.
- 20 Smith SJ, Roberts RM, Markandu ND, MacGregor GA. Potassium: the kitchen revisited. *Lancet* 1983;ii:362-3.
- 21 Kurtz TW, Morris RC. Dietary chloride as a determinant of "sodium-dependent" hypertension. *Science* 1983;222:1139-41.
- 22 Julian BA, Galla JH, Guthrie GP, Kotchen TA. Renin and aldosterone responses to short-term NaCl or NaHCO₃ loading in man. *J Lab Clin Med* 1982;100:261-8.
- 23 Rouse IL, Beilin LJ, Armstrong BK, Vandongen R. Blood-pressure-lowering effect of a vegetarian diet: controlled trial in normotensive subjects. *Lancet* 1983;ii:5-10.
- 24 Puska P, Iacono JM, Nissinen A, et al. Controlled, randomised trial of the effect of dietary fat on blood pressure. *Lancet* 1983;ii:1-5.

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SHORT REPORTS

Water intoxication and oxytocin

To reduce the time needed for induced abortions some workers have suggested using intravenous oxytocin in 5% dextrose in addition to extra-amniotic prostaglandin E₂.¹ This technique is popular and regarded as safe. I report on two patients who developed water intoxication during mid-trimester therapeutic abortions.

Case reports

CASE 1

A 31 year old woman (gravida 6, para 4) was admitted for therapeutic abortion in the 15th week of pregnancy. She was a healthy married white woman who had had one of her previous pregnancies terminated in the 12th week of gestation without complications. On admission clinical examination, full blood count, and estimation of serum electrolyte concentrations were carried out; the results were normal. At midday on the day of admission extra-amniotic instillation of 200 μ g Dinoprostone (prostaglandin E₂) by syringe pump two hourly and intravenous oxytocin 32 IU in 5% dextrose solution by IVAC pump were started. After 35 hours she became restless and confused and had a grand mal convulsion. On examination her pupils were widely dilated and unresponsive to light. Tendon reflexes were uniformly brisk and plantar responses extensor. After vaginal examination the Foley catheter and some products of conception were extracted from the introitus.

Diazepam 10 mg intravenously and oxygen 4-6 l/min via MC mask were given. The intravenous oxytocin in 5% dextrose infusion was stopped. Total fluid intake was 2.5 litres with 80 IU oxytocin, and fluid output was two litres urine and 100 ml vomit. Serum sodium concentration was 115 mmol(mEq)/l, urea 3.0 mmol/l (18 mg/100 ml), potassium 3.3 mmol(mEq)/l, haemoglobin 13.4 g/dl, and packed cell volume 0.27. After two hours of treatment with intravenous 1.8% saline, intramuscular frusemide 60 mg, and methylprednisolone 1 g she had a second seizure. Her condition remained critical until she regained consciousness after 42 hours of intensive care.

CASE 2

A 23 year old woman (gravida 2, para 1) was in the 14th week of pregnancy when a therapeutic abortion was carried out. There was no relevant medical or obstetric history. Physical and pelvic examinations were normal. Body weight was 53 kg.

On the day of her admission to hospital extra-amniotic prostaglandin E₂ instillation and intravenous oxytocin infusion were started. After 22 hours she developed uterine colic, for which intramuscular pethidine hydrochloride 150 mg was given. An hour later she had a grand mal fit and aborted. Physical examination showed widely dilated pupils that responded sluggishly to light. Tendon reflexes were brisk and plantar responses extensor. There was no papilloedema. Blood pressure was 90/60 mm Hg and the pulse rate 72/min. Because of central cyanosis oxygen 4 l/min was administered via MC mask. Diazepam 20 mg and frusemide 40 mg were given by intramuscular injections. The intravenous oxytocin in 5% dextrose was stopped. Total fluid intake was 2.7 litres with 93 IU oxytocin. The urinary output was 2.02 litres. Serum sodium concentration was 121 mmol/l, potassium 2.6 mmol/l, urea 2.8 mmol/l (16.8 mg/100 ml), haemoglobin 13.7 g/dl, and packed cell volume 0.40. Intravenous 1.8% saline at 75 ml/h was given. After 12 hours of intensive care she regained consciousness and electrolyte concentrations returned to normal.

Comment

Water intoxication in gynaecological practice is rare. Non-specific symptoms such as headache, vomiting, and restlessness preceding convulsions may often be overlooked. Biochemically, hyponatraemia occurs with serum sodium concentrations below 120 mmol/l. Although the aetiology of the condition is still not clear, it has been attributed to haemodilution due to an overload of water containing 5% dextrose. In some cases, however, the hyponatraemia cannot be explained on the basis of dilution factor alone.

Some workers have postulated other mechanisms such as the antidiuretic effect of infusion of oxytocin² and pethidine and morphine.³ I suggest that the use of 5% dextrose in water as a vehicle for oxytocin should be abandoned and that automatic infusion systems should be used to keep infused fluid to a minimum volume.

I thank Mr J Hamlett and Mr A Williams for permission to publish details of their patients, and Dr R S Ramaiah for his help.

- 1 Embrey MP, Hillier K, Mahendran P. Induction of abortion by extra-amniotic prostaglandin E₂ and F_{2 α} . *Br Med J* 1972;iii:146-9.
- 2 Abdul-Karim RW, Ritz PT. The effect of oxytocin on renal hemodynamics, water and electrolyte excretion. *Obstet Gynecol Surv* 1970;25:805-13.
- 3 Liggins GC. Anti-diuretic effect of oxytocin, morphine and pethidine in pregnancy and labour. *Aust NZ J Obstet Gynaecol* 1963;3:81-3.

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Wrexham District General Hospital, Wrexham, Clwyd LL13 7TD
F TOM MWAMBINGU, MRCOG, DCH, registrar in obstetrics and gynaecology

Correspondence to: Department of Obstetrics and Gynaecology, King Saud University, PO Box 7805, Riyadh, Kingdom of Saudi Arabia.

Fatal multisystemic toxicity associated with prophylaxis with pyrimethamine and sulfadoxine (Fansidar)

Prophylaxis for malaria is fraught with difficulty, although recent reviews have attempted to clarify indications and drug regimens.^{1 2} We describe a healthy woman who developed a fatal multisystemic illness after taking pyrimethamine and sulfadoxine (Fansidar).

Case report

A 60 year old woman with no history of allergy was prescribed Fansidar one tablet and chloroquine sulphate 400 mg weekly one week before leaving for a tour of Bangkok, Singapore, and Hong Kong. One week after departure she developed a fever with non-bloody diarrhoea and vomiting. In Singapore she was treated with intravenous fluids for dehydration and gastroenteritis. In Hong Kong she developed jaundice with urobilinogenuria, having taken

three Fansidar tablets. She was advised to end her holiday after only two weeks. She had no history of contact with jaundice, and the other members of her party were well.

Her gastrointestinal upset had settled by the time she arrived in Nottingham. On admission to hospital she was not jaundiced but was dehydrated with a temperature of 38.5°C. Analysis of her urine showed a trace of albumin and microscopic haematuria. Investigations showed creatinine concentration 83 $\mu\text{mol/l}$ (0.94 mg/100 ml), alkaline phosphatase activity 809 IU/l, bilirubin concentration 11 $\mu\text{mol/l}$ (0.64 mg/100 ml), alanine aminotransferase activity 89 IU/l, and prothrombin time 14 seconds. She developed progressive jaundice during the first week (bilirubin concentration increased to 385 $\mu\text{mol/l}$ (22.5 mg/100 ml)), results of the tests of her liver enzymes deteriorated (alkaline phosphatase activity increased to 1468 IU/l,

Liver biopsy specimen showing inflamed portal tract (top) and well preserved centrilobular zone (bottom). Haematoxylin and eosin $\times 315$ (original magnification).

and alanine aminotransferase activity to 560 IU/l), and prothrombin time increased to 25.5 s. She had evidence of pancreatic dysfunction (blood glucose concentration was 70 mmol/l (1261 mg/100 ml)), and deteriorating biochemical renal function (creatinine concentration 242 $\mu\text{mol/l}$ (2.7 mg/100 ml)), and a spreading maculopapular skin eruption.

During the next week she was delirious and had hepatic and oliguric renal failure. The skin eruption progressed to a bullous epidermal necrolysis affecting the whole body and was associated with oral and genital ulceration. Cultures of blood, urine, faeces, liver, and bone marrow yielded negative results; microscopic examination of faeces, sputum, and blood films was not helpful; and serological investigations for viruses, bacteria, and parasites also yielded negative results. Histological examination of a needle biopsy specimen of her liver (figure) showed preserved lobular architecture with a portal infiltrate of inflammatory cells containing an excess of eosinophils and extensive focal hepatocyte necrosis. Skin biopsy showed all the histological features of the subepidermal type of Lyell's syndrome (toxic epidermal necrolysis).

Supportive treatment was given including high dose steroids, but her deterioration continued and she died two weeks after admission, four weeks after becoming ill. A postmortem examination showed confluent skin bullae, liver histology as described, oedematous kidneys, and fibrinous pericarditis. Further viral, serological, and microbiological investigations yielded negative results.

Comment

This patient suffered a short fatal illness that was related to prophylactic use of Fansidar. An extensive search while she was alive and after death failed to find an aetiology other than this drug.

Skin, liver, and renal toxicity with fever are well known idiosyncratic reactions to sulphonamides. They have occurred separately in patients after use of Fansidar^{3,4} and are presumably due to the sulphadoxine (a long acting sulphonamide). No other cases have been reported in which all these toxic manifestations have occurred in the same patient. We have reported this case to the Committee on the Safety of Medicines and to the manufacturer.

We thank Professor J R Hampton for permission to report his case and Mr Bill Brackenbury for the photography.

- 1 Public Health Laboratory Service Malaria Reference Laboratory. Malaria prophylaxis. *Br Med J* 1983;286:787-9.
- 2 Public Health Laboratory Service Malaria Reference Laboratory. Malaria prophylaxis: two problem regions. *Br Med J* 1984;288:1216.
- 3 Olsen VV, Loft S, Christensen KD. Serious reactions during malaria prophylaxis with pyrimethamine-sulfadoxine. *Lancet* 1982;ii:994.
- 4 Whitfield D. Presumptive fatality due to pyrimethamine-sulfadoxine. *Lancet* 1982;ii:1272.

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Departments of Medicine and Histopathology, University Hospital, Nottingham NG7 2UH

C D SELBY, BMEDSCI, BM, senior house officer in medicine
E J LADUSANS, BSC, MRCP, registrar in medicine
P G SMITH, FRCPATH, consultant in histopathology

Correspondence to: Dr C D Selby, Department of Neurology, University Hospital, Nottingham NG7 2UH.

Cryptosporidiosis in Bangladesh

Despite the large number of enteropathogens identified in recent years the cause of many episodes of diarrhoea remain undetermined. The protozoan *Cryptosporidium* was first described as a pathogen causing diarrhoea in animals in 1907, and in man in 1976.¹ We were able to identify the cause for diarrhoea in only two thirds of patients coming to our clinic.² Cryptosporidiosis is an emerging zoonotic disease, and we therefore began screening for cryptosporidial oocysts in stools of patients visiting our clinic as part of a surveillance programme.²

Methods and results

At the Dacca clinic we screened 4% of patients with diarrhoea for cryptosporidial oocysts, using Giemsa stain on faecal smears.³ All specimens were examined for other common enteropathogens. Thirty eight of 578 smears collected from 1 January to 31 May 1984 were judged to be positive, based on the finding of characteristic oocysts—that is, "holes" in the stained background. These unstained areas sometimes have a faint blue centre with fine red or purple corpuscles.³ Replicate smears made from refrigerated faeces were stained by a modified acid fast technique⁴; 25 were found to be positive (4.3% of 578 samples).

Eighteen of the 25 patients with cryptosporidiosis were children aged under 2. The disease was found in both sexes and in 21 patients who were moderately to well nourished. *Cryptosporidium* was the only pathogen in 20 of the 25 patients. Twenty four of them had watery diarrhoea, and 18 were either mildly dehydrated or not dehydrated at all three days after the start of diarrhoea. Six of the 18 children under 2 were moderately dehydrated. Twenty two patients suffered from vomiting and three from mild fever. There was a sudden increase in cases of cryptosporidiosis during the hot, humid weather in March.

In most stool samples we found few segmented leukocytes, no other inflammatory cells, and no red blood cells. All dehydrated patients were successfully rehydrated orally with a rice based solution, and 18 were discharged within 16 hours of admission. A cough was present in six of the patients under 2.

Comment

By studying a small sample of patients we have established that *Cryptosporidium* exists in Bangladesh. As the sole pathogen it seems to cause a mild, transient, easily managed form of diarrhoea, particularly among young children; only four (16%) of the 25 patients studied were malnourished. The presence of cough in some of the